## <u>Remarks</u>

Applicants submit that claim 10 has been further limited by incorporating the limitations of dependent claims 15 and 16. Thus, claims 15 and 16 have been canceled. Claims 17-21 and 35, previously depending from claims 15 or 16, have been amended to depend from claim 10. Applicants submit that the subject matter of claim 10 as presently recited has been previously examined and thus, no new search is necessary. No new matter is added by way of the amendment and its entry is respectfully requested.

## Rejections under 35 U.S.C. § 112

The Examiner has maintained the rejection of claims 10, 12, and 14-19 based on failure to comply with the enablement requirement under 35 U.S.C. 112, first paragraph. The Examiner alleges that one of skill in the art would not predictably be able to reduce the invasivity of cancer cells that are susceptible to AXL suppression in vivo. Applicants disagree with the Examiner's allegation and submit herewith references, Voskoglou-Nomikos et al. (Clinical Research, vol. 9, 4227-4239, 2003) and Khleif et al. (Animal Models in Developmental Therapeutics, Chapter 42, p. 573-584, 2000), in support of the enablement of those skilled in the art to use the presently claimed methods at the time the invention.

Voskoglou-Nomikos et al. assess the clinical predictive value of the in vitro cell line, human xenograft, and mouse allograft pre-clinical models. The results suggest that the in vitro cell line model is of at least equivalent usefulness to the human xenograft model (see page 4237, left column, second paragraph). Further, the authors

argue for "emphasis to be placed on in vitro cell lines (in the context of the NCI Human Tumor Cell Line Screen) and appropriate panels of the human xenograft model."

Khleif et al. discuss the role of animal models in drug discovery and drug screening. The reference describes that National Cancer Institute's (NCI) current cancer screening method as "an in vitro (Stage I) screen followed by the more refined in vivo (Stage II) screen" (see paragraph bridging pages 573-574). In particular, it can be seen from this reference that the implantation of tumor cells is a generally accepted model for drug development. Further, the authors describe several approaches for tumor implantation (pages 577-578). On page 576, right column, 3<sup>rd</sup> full paragraph, Khleif et al. refer to the success of human tumor xenografting into nude mice as "revolutionizing many aspects of cancer research, including drug development." The reference further states "in fact, excellent correlations can be made between average growth delay for human tumors in nude mice treated with the best available drug combinations and complete clinical response rates"; studies using lung cancer, colon cancer, breast cancer, and malignant melanoma are cited (see page 577, 1st full paragraph). Moreover, Khleif et al. discuss the refinement of animal models in drug development over time, mentioning the "general convertability of doses between species" (see page 581, right column, last paragraph). Based on the above reasoning, Applicants believe that claim 10 is allowable and claims 12, and 14-19, depending from claim 10, are allowable for at least the above reasons. Applicants request that the rejection be withdrawn and that claims 10, 12, and 14-19, and 35 be allowed.

Claims 10, 12, 14-19, and 35 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite. The Examiner asserts that the term "cancer cells that are susceptible to Axl suppression" is not defined by the claim and the specification does not teach what the term means. Furthermore, claims 10, 12, 14-19, and 35 were rejected under 35 U.S.C. 112, first paragraph for failing to comply with the written description requirement. The Examiner asserts that the limitation of "cancer cells that are susceptible to AxI suppression" has no clear support in the specification. Claim 10 has been amended to delete the recitation "cancer cells that are susceptible to Axl suppression" and to specifically name cancer cells selected from the group consisting of breast cancer cells, prostate cancer cells, kidney cancer cells, glioblastoma cells or cancer cells of epithelial origin. Support for this amendment can be found in the specification on page 4, lines 4-10. Based on the above reasoning, Applicants believe that claim 10 is allowable and claims 12, 14-19 and 35, depending from claim 10, are allowable for at least the above reasons. Applicants request that the rejection be withdrawn and that claims 10, 12, 14-19, and 35 be allowed.

## Rejections under 35 U.S.C. § 102

Claims 10, 12, and 14 were rejected under 35 U.S.C. §102(b) as being anticipated by Liu (U.S. 5,468,634). The Examiner acknowledges that Liu does not specifically state that contacting tumor cells with Axl antibodies are a method of reducing the invasivity of cancer cells that are susceptible to AXL suppression; however, he asserts that the presently claimed method appears to be the same as Liu.

Applicants submit that there is no teaching or suggestion in Liu that relates to a method of reducing invasivity. Liu relates to diagnostic assays for detecting a tumor and only mentions in passing that Axl antibodies may be used for therapeutic purposes. Thus, Liu does not disclose or suggest each element of claim 10 and therefore does not anticipate or render obvious the presently claimed invention. Furthermore, claim 10 has been further limited by incorporation of the limitations of claims 15 and 16, which are not anticipated by Liu. Thus, Applicants believe that claim 10 is allowable and claims 12, and 14, depending from claim 10, are allowable for at least the above reasons. Applicants request that the rejection be withdrawn and that claims 10, 12, and 14 be allowed.

In view of the above amendments and remarks hereto, Applicants believe that all of the Examiner's rejections set forth in the May 14, 2008 Office Action have been fully overcome and that the present claims fully satisfy the patent statutes. Applicants, therefore, believe that the application is in condition for allowance. The Director is authorized to charge any fees or overpayment to Deposit Account No. 02-2135.

The Examiner is invited to telephone the undersigned if it is deemed to expedite allowance of the application.

Respectfully submitted,

Ву

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